

CLAIMS

We claim:

1. A method for detecting the presence of a target sequence in a nucleic acid sample, comprising
 - 5 a) applying a first input signal comprising an AC component and a non-zero DC component to a hybridization complex, said hybridization complex comprising at least a target sequence and a first probe single stranded nucleic acid, said hybridization complex being covalently attached to:
 - i) a first electron transfer moiety comprising an electrode; and
 - 10 ii) a second electron transfer moiety; and
 - b) detecting the presence of said hybridization complex by receiving an output signal characteristic of electron transfer through said hybridization complex.
2. A method for detecting the presence of a target sequence in a nucleic acid sample, comprising
 - 15 a) applying a first input signal comprising an AC component at a first frequency and a non-zero DC component to a hybridization complex, said hybridization complex comprising at least a target sequence and a first probe single stranded nucleic acid, said hybridization complex being covalently attached to:
 - i) a first electron transfer moiety comprising an electrode; and
 - 20 ii) a second electron transfer moiety;
 - b) applying a second input signal comprising an AC component at least a second frequency and a non-zero DC component to said hybridization complex; and
 - c) detecting the presence of said hybridization complex by receiving an output signal characteristic of electron transfer through said hybridization complex.
- 25 3. A method for detecting the presence of a target sequence in a nucleic acid sample, comprising
 - a) applying a first input signal comprising an AC component and a first non-zero DC component to a hybridization complex, said hybridization complex comprising

at least a target sequence and a first probe single stranded nucleic acid, said hybridization complex being covalently attached to:

i) a first electron transfer moiety comprising an electrode; and

ii) a second electron transfer moiety;

- 5 b) applying a second input signal comprising said AC component and at least a second non-zero DC component to said hybridization complex; and
 c) detecting the presence of said hybridization complex by receiving an output signal characteristic of electron transfer through said hybridization complex.

10 4. A method for detecting the presence of a target sequence in a nucleic acid sample, comprising

a) applying a first input signal comprising an AC component at a first voltage amplitude

to a hybridization complex, said hybridization complex comprising at least a target sequence and a first probe single stranded nucleic acid, said hybridization complex being
15 covalently attached to:

i) a first electron transfer moiety comprising an electrode; and

ii) a second electron transfer moiety;

b) applying a second input signal comprising said AC component at a second voltage amplitude to said hybridization complex; and

20 c) detecting the presence of said hybridization complex by receiving an output signal characteristic of electron transfer through said hybridization complex.

5. A method according to claim 4 wherein said input signals further comprise a non-zero DC component.

25 6. A method according to claims 1, 2, 3 or 4, wherein said hybridization complex comprises

a) a single stranded nucleic acid covalently attached to:

1) a first electron transfer moiety comprising an electrode; and

2) a second electron transfer moiety; and

b) a target sequence hybridized to said single stranded nucleic acid.

7. A method according to claims 1, 2, 3 or 4 wherein said hybridization complex comprises:

- a) a single stranded nucleic acid covalently attached via a conductive oligomer to a first electron transfer moiety comprising an electrode; and
- 5 b) a target sequence hybridized to said single stranded nucleic acid; and
 - i) a second electron transfer moiety.

8. A method according to claims 1, 2, 3 or 4 wherein said output signal comprises a current.

10 9. A method according to claims 1, 2, 3 or 4 wherein said output signal comprises a voltage.

10. A method according to claims 1, 2, 3 or 4 wherein said output signal comprises a phase shift between said input and said output signals.

15 11. A method according to claims 1, 2, 3 or 4 wherein said output signal comprises a change in the faradaic impedance between the electron transfer moieties as a result of the formation of the hybridization complex.

12. A method according to claims 1, 2, 3 or 4 further comprising adding said target sequence to said single stranded nucleic acid to form said hybridization complex.

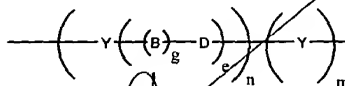
13. A method according to claims 1, 3 or 4 further comprising applying input signal at a plurality of frequencies.

20 14. A method according to claims 1, 2 or 4 further comprising applying signal at a plurality of DC voltages.

15. A method according to claims 1, 2, 3 or 4 wherein said single-stranded nucleic acid is covalently attached to said electrode via a spacer.

16. A method according to claim 15, wherein said spacer is a conductive polymer.

17. A method according to claim 15, wherein said conductive polymer has the formula:



wherein

Y is an aromatic group;

5 n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

m is zero or 1;

wherein when g is 1, B-D is a conjugated bond; and

10 wherein when g is zero, e is 1 and D is preferably carbonyl, or a heteroatom moiety,
wherein the heteroatom is selected from oxygen, sulfur, nitrogen or phosphorus.

18. A method according to claim 15, wherein said electrode further comprises a monolayer.

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19. An apparatus for the detection of target nucleic acids in a test sample, comprising:

- a) a test chamber comprising a first and a second measuring electrode, wherein said first measuring electrode comprises a covalently attached conductive oligomer covalently attached to a single stranded nucleic acid; and
- b) an AC/DC voltage source electrically connected to said test chamber.

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20. An apparatus for the detection of target nucleic acids in a test sample, comprising:

- a) a test chamber comprising a first and a second measuring electrode, wherein said first measuring electrode comprises a covalently attached single stranded nucleic acid comprising a covalently attached second electron transfer moiety; and
- b) an AC/DC voltage source electrically connected to said test chamber.

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21. An apparatus according to claim 19 or 20, further comprising:

- d) a processor coupled to said electrodes.

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22. An apparatus according to claim 19 or 20, wherein said AC voltage source is capable of delivering frequencies from between about 1 Hz to about 100 kHz.

23. An apparatus according to claim 22, wherein said single stranded nucleic acids are covalently attached to said electrode via a spacer.

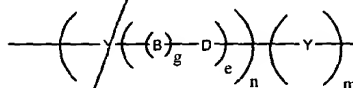
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24. An apparatus according to claim 23, wherein said spacer is a conductive oligomer.

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25. An apparatus according to claim 19 or 24, wherein said conductive oligomer has the formula:



wherein

Y is an aromatic group;

10 n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

m is zero or 1;

wherein when g is 1, B-D is a conjugated bond; and

15 wherein when g is zero, e is 1 and D is preferably carbonyl, or a heteroatom moiety,

wherein the heteroatom is selected from oxygen, sulfur, nitrogen or phosphorus.

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